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EXAMINER	
LU, FRANK WEI MIN	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 05/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/831,142	CAMPBELL, ANTHONY KEITH	
	Examiner	Art Unit	
	Frank W Lu	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-30* is/are pending in the application.

4a) Of the above claim(s) *11-14,18-26 and 28-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,15-17 and 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *11/2004* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

1. Applicant's election with traverse of Group IA, claims 1-10, 15-17, and 27, and SEQ ID NO: 1 filed on February 12, 2004 is acknowledged. The traversal is on the ground(s) that: (1) "The International Examiner found no lack of unity, applying the same legal standard to the identical facts. As a result, applicant believes that the U.S. Patent Office cannot now contend that examination of all the pending claims in the present application would pose an undue searching burden. Indeed, the Examiner has a considerable benefit of the search results generated by the International Examiner, on the basis of the pending claims."; (2) "the Official Action does not explain why, standard to the identical claims, the opposite result is now being reached the present U.S. national phase application relative to the international application."; (3) "[A]s to the sequence election requirement, the Examiner is respectfully reminded that the U.S. Patent and Trademark Office publishes its policy for the examination of patent applications containing sequence listings Official Gazette, 11920.g.68 (November 19, 1996). Applicant notes that in establishing the new policy, the Commissioner has partially waived the requirements of 37 CFR 51.41 and put a reasonable number of sequences claimed and examined a single application. Under this policy, up to ten sequences may be examined single application without restriction. Indeed, applicant believes that an examination of the sequences found in the present claims order."; and (3) "[A]t the very least, applicant respectfully submits that SEQ ID NOs. 1-3 should be examined together. SEQ ID NOs. 1-3 are directed to CDNAS which functionally very similar and of approximately equal length. As a result, applicant does believe that the examination of

SEQ ID NOs. 1-3 places a burden on the Examiner and respectfully requests the examination of SEQ ID NOs.".

The above arguments have been fully considered and have not been found pervasive toward the withdrawal of the restriction requirement nor pervasive toward the relaxation of same such that Groups IA and IB will be examined together. First, since this case is a 371 case, an undue searching burden argued by applicant is not the reason for the restriction. The restriction is based on that Groups IA and IB are no longer linked by a special technical feature since an isolated, purified recombinant nucleic acid sequence recited in (b) of claim 1 is known in the art, (for example, see Baba et al., (Anal. Chem., 64, 1920-1925, 1992, see poly T in page 1922). Second, although, in PCT application of this instant application, the examiner from European Patent Office did not restrict Groups IA and IIB, there is no policy in US Patent Office to indicate that the restriction made by US Patent Office must follow guidance from European Patent Office. Third, although the examiner agrees that "up to ten sequence may be examined in a single application without restriction", this does not mean that the examiner must examine ten nucleotide sequences together. Although SEQ ID Nos:1-3 are directed to cDNA, these nucleotides are directed to different proteins that are distinct each other. According to MPEP 803.04, "[B]y statute, '[i]f two or more independent and distinct inventions are claimed in one application, the Commissioner may require the application to be restricted to one of the inventions.' 35 U.S.C. 121. Pursuant to this statute, the rules provide that '[i]f two or more independent and distinct inventions are claimed in a single application, the examiner in his action shall require the applicant . . . to elect that invention to which his claim shall be restricted.' 37

CFR 1.142(a). See also 37 CFR 1.141(a).". Since SEQ ID Nos:1-3 are directed to cDNAs of different proteins, the requirement is deemed proper and is therefore made FINAL.

Specification

2. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. The cover paper of WO 00/28025 cannot be considered as an abstract.

3. The disclosure is objected to because of the following informalities: applicant needs to add "BRIEF DESCRIPTION OF THE FIGURES" in page 4; and (2) there are several amino acid sequences with 4 or more amino acids in the specification (see Table 1 in page 6, pages 7, 8, 11, 12, and 20). However, these sequences have no SEQ ID Nos.

Appropriate correction is required.

Claim Objections

4. Claim 1 is objected to because of the following informalities: (1) "r" in the first line of the claim should be "or"; and (2) "that hybridizes" in (b) and (c) of the claim should be "a sequence that hybridizes".

5. Claim 3 is objected to because of the following informality: SEQ ID Nos: 2-6 and 23 should be deleted since only SEQ ID NO: 1 is selected.

6. Claims 4, 5, 8-10, and 15-17 are objected to because of the following informality: "according to" should be "from".

7. Claim 8 is objected to because of the following informality: "a construct" should be "the construct".

8. Claim 17 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim because, although plasmid recited in claim 15 is a vector, a vector (any kind of vector) recited in claim 17 is much broader than the plasmid recited in claim 15. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

9. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

10. Written Description

Claims 1, 4-10, and 15-17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Applicant is referred to the interim guidelines on written description published on December 21, 1999 in the Federal Register at Volume 64, Number 244, pp.71427-71440.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed.". *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116.

The specification (page 50 and sequencing listing) provides adequate written descriptions for SEQ ID NO: 1, which is cDNA of apopholasin from bivalve mollusk *pholas dactylus* wherein apopholasin is an apoprotein of pholasin (a luminescent protein) (see the specification, page 3 and sequencing list). However, the specification fails to adequately describe an isolated nucleic acid sequence from any kind of source that encodes apopholasin as recited in claims 1, 4, 5, 9, and 15-17 and an isolated construct that encodes any kind of apophotoprotein with properties recited in claims 6 and 7. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells, Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998).

In this instant case, although the specification adequately describes for SEQ ID NO: 1, which is cDNA of apopholasin from bivalve mollusk *pholas dactylus* (see the specification, page 3 and sequencing listing), the specification fails to adequately describe an isolated nucleic acid sequence from any kind of source that encodes apopholasin as recited in claims 1, 4, 5, 9, and 15-17 and an isolated construct that encodes any kind of apophotprotein with properties recited in claims 6 and 7. Since claim 1 can be read as an isolated nucleic acid sequence that encodes apopholasin from any kind of source, and the specification does not show that, besides bivalve mollusk *pholas dactylus,* other organisms such as human and mice also have apopholasin. It is unclear, besides bivalve mollusk *pholas dactylus,* other organisms such as human and mice also have apopholasin. Furthermore, since claims 6 and 7 do not limit source of the isolated construct that encodes any kind of apophotprotein with properties recited in claims 6 and 7, it is unclear, besides bivalve mollusk *pholas dactylus,* other organisms such as human and mice, also have an apophotoprotein with properties recited in claims 6 and 7. Therefore, the general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed.

With limited disclosure provided by the specification, the skilled artisan cannot envision all above possible isolated nucleic acids and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel,* 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co.* Ltd., 18 USPQ2d 1016 (Fed. Cir. 1991).

One cannot describe what e has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

11. Enablement

Claims 15 and 17 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for producing cell, plasmid or virus comprising an isolated sequence that encodes apopholasin, does not reasonably provide enablement for: (1) producing any kind of living organism comprising an isolated sequence that encodes apopholasin; and (2) producing any kind cell, plasmid, virus or live organism comprising substantially homologous to an isolated sequence that encodes apopholasin The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

In *In re Wands*, 858 F.2d 731,737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988) the court considered the issue of enablement in molecular biology. The Court summarized eight factors to be considered in a determination of "undue experimentation". These factors include: (a) the quantity of experimentation necessary; (b) the amount of direction or guidance presented; (c) the presence or absence of working examples; (d) the nature of the invention; (e) the state of the prior art; (f) the relative skill of those in the art; (g) the predictability of the art; and (h) the

breadth of the claims. The Court also stated that although the level of skill in molecular biology is high, results of experiments in molecular biology are unpredictable.

To begin, there is no direction or guidance in the specification to produce any kind of living organism comprising an isolated sequence that encodes apopholasin and produce any kind cell, plasmid, virus or live organism comprising substantially homologous to an isolated sequence that encodes apopholasin. While the relative skill in the art is very high (the Ph.D. degree with laboratory experience), there is no predictability whether any kind of living organism comprising an isolated sequence that encodes apopholasin and any kind cell, plasmid, virus or live organism comprising substantially homologous to an isolated sequence that encodes apopholasin can be produced by the method recited in claims 15 and 17.

Claims 15 and 17 are directly to any kind of living organism comprising an isolated sequence that encodes apopholasin and any kind cell, plasmid, virus or live organism comprising substantially homologous to an isolated sequence that encodes apopholasin. The specification only describes to produce cell, plasmid or virus comprising an isolated sequence that encodes apopholasin (see the specification, pages 16-28). However, the specification does not provide a guidance to produce any kind of living organism comprising an isolated sequence that encodes apopholasin and produce any kind cell, plasmid, virus or live organism comprising substantially homologous to an isolated sequence that encodes apopholasin. First, although the specification indicates that transgenic animals such as transgenic mice can be generated from apopholasin cDNA, the specification does not provide an evidence to show that a transgenic mouse of apopholasin has made. It is known that the state of the art in the fields of transgenic animal at the time of the invention was unpredictable, the transgene expression and resulting phenotype of

such expression is not always accurately predictable. For example, Sigmund, June 2000 (Arterioscler. Thromb. Vasc. Biol., p. 1425-1429), reports that variation in the genetic background contributes to unpredictable resulting phenotypes of transgenic or gene-targeted animals. "Animals containing the same exact genetic manipulation exhibit profoundly different phenotypes when present on diverse genetic backgrounds, demonstrating that genes unrelated, per se, to the ones being targeted can play a significant role in the observed phenotype" (abstract). Sigmund further states that "many of the phenotypes examined in transgenic and knockout models are influenced by the genetic background in which they are studies...Although all mouse strains contain the same collection of genes, it is allelic variation...and the interaction between allelic variants that influence a particular phenotype. These "epigenetic" effects can dramatically alter the observed phenotype and therefore can influence or alter the conclusions drawn from experiments" (e.g. introduction). Second, claim 15 does not limit to transgenic animal since live organism recited in claim 15 can be any kind of organism such as human. Until now, there is no evidence to show that a transgenic human has been made. Third, since claim 15 is directed to any kind of cell, plasmid, virus or live organism comprising substantially homologous to an isolated sequence that encodes apopholasin and the specification does not provide any kind of sequence that is substantially homologous to an isolated sequence that encodes apopholasin, it is impossible to make any kind cell, plasmid, virus or live organism comprising substantially homologous to an isolated sequence that encodes apopholasin.

With these unpredictable factors, the skilled artisan will have no way to predict the experimental results. Accordingly, it is concluded that undue experimentation is required to make the invention as it is claimed. These undue experimentation at least includes to test

whether any kind of living organism comprising an isolated sequence that encodes apopholasin and any kind cell, plasmid, virus or live organism comprising substantially homologous to an isolated sequence that encodes apopholasin can be produced.

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. Claims 1-10, 15-17, and 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

14. Claim 1 is rejected as vague and indefinite because it is unclear that apopholasin in parentheses of (a) further limits the apophotoprotein of pholasin or not. If apopholasin in parentheses of (a) further limits the apophotoprotein of pholasin, claim 1 and claim 8 do not correspond each other since claim 8 further limits apophotoprotein. Please clarify.

15. Claim 1 recites the limitation "sequence (a)" in (b) and (c) of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no sequence (a) in (a) of the claim. Please clarify.

16. Claim 1 recites the limitation "the sequences (a), (b) or (c)" in (d) of the claim. There is insufficient antecedent basis for this limitation in the claim because there is no sequences (a), (b) or (c) in (a) to (c) of the claim. Please clarify.

17. Claim 1 is rejected as vague and indefinite in view of the phrase "an oligonucleotide specific for any of the sequences (a), (b) or (c) PROVIDED THAT such homologous sequences according to (b) or (c) encode a protein capable of binding to luciferin" because, from the claim,

there is no correlation between an oligonucleotide specific for any of the sequences (a), (b) or (c) and homologous sequences that encode a protein capable of binding to luciferin. Please clarify.

18. Claim 1 is rejected as vague and indefinite because the phrase "but for the degeneracy of the genetic code" in (a) is confusing since there is no correlation between a sequence and the degeneracy of the genetic code. Please clarify.

19. The term "stringent conditions" in claim 1 is a relative term which renders the claim indefinite. The term "stringent conditions" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. Note that the specification does not define "stringent conditions". Please clarify.

20. Claim 2 is rejected as vague and indefinite because it is unclear that SEQ ID NO: 1 in parentheses further limits apopholasin or not. Please clarify.

21. Claim 3 is rejected as vague and indefinite because it is unclear that SEQ ID NOs: 1-6 and 23 in parentheses further limits apopholasin or not. Please clarify.

22. Claim 6 is rejected as vague and indefinite in view of the phrase "whose expression in a substrate, in association with a luciferin therefor, signals the presence of oxygen or an oxygen metabolite in the substrate" because this phrase is not a complete sentence and does not make sense. Please clarify.

23. Claim 7 is rejected as vague and indefinite in view of the phrase "whose expression in a substrate, in association with a luciferin therefor, signals the presence of oxygen or an oxygen metabolite in the absence of a corresponding luciferase in the substrate" because this phrase is not a complete sentence and does not make sense. Please clarify.

24. Claim 9 recites the limitation " a recombinant construct" in the claim. There is insufficient antecedent basis for this limitation in the claim because there is no "a recombinant construct" in claim 1. Please clarify.

25. Claim 27 provides for the use of a sequence or a protein, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 27 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 101

26. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claim 14 is rejected under 35 U.S.C. 101 because they are directed to non-statutory subject matter. The claim encompasses human beings (living organism), which is not considered patentable subject matter. See MPEP 2105. This rejection could be overcome by amending the claim to recite a "non-human transgenic animal".

Claim Rejections - 35 USC § 102

27. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

28. Claims 1 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Scheele *et al.*, (US Patent No. 5,643, 766, published on July 1, 1997).

Scheele *et al.*, teach synthesis of full-length, double-stranded DNA from a single stranded linear DNA template.

Regarding claims 1 and 10, Scheele *et al.*, teach a Poly (dT) primer with 5-30 T (see column 5, Table 1 and lines 55-57). When the Poly (dT) primer with 18 T, this primer is completely hybridize with 18 A in 3' end of SEQ ID NO: 1 of this instant application. Since SEQ ID NO: 1 of this instant application is a sequence that encodes apopholasin (see claim 2 of this instant application), Scheele *et al.*, disclose a sequence (ie., the Poly (dT) primer with 18 T) that hybridizes to a sequence in (a) of claim 1 under stringent conditions as recited in (b) of claim 1. Since the Poly (dT) primer is a DNA, claim 10 is anticipated by Scheele *et al.*.

Therefore, Scheele *et al.*, teach all limitation recited in claims 1 and 10.

29. Claims 1, 6, 7, 10, and 15-17 are rejected under 35 U.S.C. 102(b) as being anticipated by Prasher *et al.*, (Biochemistry, 26, 1326-1332, 1987).

Prasher *et al.*, teach sequence comparisons of complementary DNAs encoding aequorin isotypes.

Regarding claims 1 and 10, Prasher *et al.*, teach cDNA sequences of apoaequorins 1-3 (AEQ1, AEQ2,and AEQ 3) (see Figure 2 in page 1328). Since (b) of claim 1 does not specify percentage of homology between an isolated, purified nucleic acid sequence and a sequence that encodes the apopholasin, ARQ 1 taught by Prasher *et al.*, is an isolated, purified nucleic acid sequence comprising a sequence substantially homologous to a sequence that encodes the apopholasin as recited in (b) of claim 1 because ARQ 1 is at least partially homologous to apopholasin. Since AEQ I encodes a polypeptide (apoaequorin) that is capable of binding to coelenterate luciferin (see page 1327, left column, second paragraph), Prasher *et al.*, disclose that such homologous sequences from (b) encodes a protein capable of binding to luciferin as recited in claim 1. Since AEQ1 is a cDNA, claim 10 is anticipated by Prasher *et al.*.

Regarding claim 6, since ARQ 1 taught by Prasher *et al.*, is an isolated, purified nucleic acid sequence that encodes apoaequorin, which is capable of binding to coelenterate luciferin or oxyluciferin (see page 1327, left column, second paragraph and Figure 2 in page 1328) and is cloned in pUC9 expression vector (see page 1327, right column, sixth paragraph), according to the description of apophotoprotein in the specification (see the specification, page 2, lines 16-24), apoaequorin is an apophotoprotein. Therefore, Prasher *et al.*, disclose an isolate, purified construct incorporating an apophotoprotein wherein expressed apophotoprotein is a substrate for luciferin and the apophotoprotein is associated with a luciferin as recited in claim 6. Since Prasher *et al.*, teach that oxidation of the luciferin leads to release of blue light from aequorin (apoaequorin-luciferin complex) (see page 1327, left column, second paragraph), Prasher *et al.*, disclose that production of signals (ie., blue light) is in the presence of oxygen or an oxygen metabolite and the substrate (ie., apoaequorin) as recited in claim 6.

Regarding claim 7, since ARQ 1 taught by Prasher *et al.*, is an isolated, purified nucleic acid sequence that encodes apoaequorin, which is capable of binding to coelenterate luciferin or oxyluciferin (see page 1327, left column, second paragraph and Figure 2 in page 1328) and is cloned in pUC9 expression vector (see page 1327, right column, sixth paragraph), according to the description of apophotoprotein in the specification (see page 2, lines 16-24), apoaequorin is an apophotoprotein. Therefore, Prasher *et al.*, disclose an isolate, purified construct incorporating an apophotoprotein wherein expressed apophotoprotein is a substrate for luciferin and the apophotoprotein is associated with a luciferin as recited in claim 7.

Regarding claims 15-17, since ARQ 1 taught by Prasher *et al.*, is an isolated, purified nucleic acid sequence that encodes apoaequorin, which is capable of binding to coelenterate luciferin or oxyluciferin (see page 1327, left column, second paragraph and Figure 2 in page 1328) and is cloned in pUC9 expression vector expressed in an E. coli strain (see page 1327, right column, sixth paragraph), Prasher *et al.*, disclose a plasmid having incorporated expressibly therein a sequence in claim 1 whereby the sequence is capable of producing an apoprotein (ie., apoaequorin) as recited in claim 15, a vector (ie., PUC9 expression vector) comprising a sequence in claim 1 as recited in claim 16, and a host cell (ie., an E. coli strain with a pUC9 expression vector having cDNA of ARQ 1) transformed or transfected with the vector in claim 16 as recited in claim 17.

Regarding claim 27, since apoaequorin encoded by ARQ 1 taught by Prasher *et al.*, is used in the immunoblot analysis (see page 1327, right column, six paragraph, and Figures 3 and 4 in pages 1329 and 1330), Prasher *et al.*, disclose the use of a protein (ie., apoaequorin) in claim 1 in the detection as recited in claim 27.

Therefore, Prasher *et al.,* teach all limitation recited in claims 1, 6, 7, 10, 15-17, and 27.

Conclusion

30. No claim is allowed.

31. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CAR § 1.6(d)). The CM Fax Center number is either (703)872-9306 or (703)305-3014.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Frank Lu, Ph.D., whose telephone number is (571)272-0746. The examiner can normally be reached on Monday-Friday from 9 A.M. to 5 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (571)272-0782.

Any inquiry of a general nature or relating to the status of this application should be directed to the Chemical Matrix receptionist whose telephone number is (703) 308-0196.

Frank Lu
PSA
May 20, 2004

FRANK LU
PATENT EXAMINER